AN A CONTRARIO APPROACH FOR OUTLIERS SEGMENTATION: APPLICATION TO MULTIPLE SCLEROSIS IN MRI.

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ABSTRACT

The detection of Multiple Sclerosis (MS) lesions in Magnetic Resonance (MR) images remains an important issue in medical image processing. Diagnostic criteria for MS based on brain MRI concern mainly dissemination in space and time. In this context, this paper describes a novel region-based approach to automatically count the number of MS lesions present in a set of MR images. Given a set of candidate regions obtained with a mean-shift based segmentation, the detection algorithm decides for each region if it is part of a MS lesion or if it belongs to non-pathologic regions (white matter (WM), grey matter (GM) or cerebro-spinal fluid (CSF)). The distribution of each brain tissue is modeled using a Gaussian Mixture Model and MS lesions are detected as outliers with respect to this model. Finally, we propose several criteria for segmentation assessment and we validate our algorithm on the BrainWeb data set. Preliminary results on clinical data are also shown.

Index Terms— MRI, *a contrario* Framework, Brain Segmentation, Multiple Sclerosis Lesions

1. INTRODUCTION

Magnetic Resonance Imaging (MRI) is currently fundamental for the monitoring and diagnosis of multiple sclerosis (MS). New diagnostic criteria for MS integrating MRI assessment with clinical methods were introduced in 2001 (the so-called "McDonald Criteria") and were recently revised to simplify and speed diagnosis, whereas maintaining sensitivity and specificity [P05]. A key point of these criteria concern the dissemination in space by MRI evidence (*i.e.* the number of MS lesions) and not the lesion load. Therefore, an automatic segmentation system able to determine the number of MS lesions appears to be very useful for diagnosis.

MS lesion segmentation task is usually performed using statistical voxel-based intensity modeling [V01, ZFE02, AAPH$^+$05]. The intensity of normal brain tissues is usually modeled by mixture of Gaussian probability distribution functions. The model consists of a Gaussian per tissue type and lesions are considered as outlier voxels. Noise removal, atlas registration techniques or local regularization (using Hidden Markov Random Field (HMRF)) can be used to improve the results, but choice of the threshold to decide which voxels correspond to outliers remains manual.

Recently, a region-based method have been proposed for brain segmentation task [JMY06] using a maximum a posteriori approach for region labeling. Less sensitive to noise, such approach is expected to be more robust than pixel-based methods to segment brain tissues structures, tumors or lesions. In this work, we propose to investigate the use of a region-based approach for MS lesion segmentation in MRI. An original unsupervised approach based on the *a contrario* framework is presented in this paper. The *a contrario* approach, recently developed by Desolneux *et al.* [DMM03], is a mathematical formalization of a perceptual grouping principle which has been successfully applied to various detection problems in computer vision: the detection of alignments and edges [DMM03], vanishing points [ADV03] or motion detection [VCB06].

Magnetic Resonance Imaging (MRI) is widely used for both qualitative and quantitative analysis of MS over time. Since MS lesions exhibit different appearances depending on the type of MR images (T_1-weighted, T_2-weighted, FLAIR), image processing algorithms have to integrate complementary information available in multimodal data. Considering multiple MR sequences (T1-weighted, T2-weighted, T2-weighted FLAIR), brain tissues are segmented into three classes : WM, GM and CSF. Distribution parameters are then used to automatically extract MS lesion regions based on the a contrario decision framework.

2. SEGMENTATION ALGORITHM

2.1. Parametric Model of Brain Tissues

In this paper, we assume that the distribution of each brain tissue (WM, GM, CSF) can be well approximated by a Gaussian law. Considering m different image modalities simultaneously, the intensity vector of each voxel $\mathbf{x_i}$ is modeled by a Gaussian Mixture Model (GMM):

$$p(\mathbf{x_i}|\Theta) = \sum_{j=1}^{k} \alpha_j \frac{(2\pi)^{m/2}}{\sqrt{|\Sigma_j|}} e^{-\frac{1}{2}(\mathbf{x_i}-\mu_j)^T \Sigma_j^{-1} (\mathbf{x_i}-\mu_j)} \quad (1)$$

where k is the number of mixture components, $\Theta = (\alpha, \mu, \Sigma)$ being the hyperparameters of the GMM (α_j the mixture proportions, μ_j and Σ_j are the mean vectors and covariance matrices of the multivariate Gaussian laws). Parameters Θ of the finite GMM are estimated within the well-defined statistical framework based on the Maximum Likelihood Estimator (MLE) using the Expectation-Maximization (EM) algorithm as optimization method and HMRF for local regularization. Based on the estimated GMM of WM, GM and CSF at this step, we will be able to detect MS lesions as outlier regions with respect to the GMM.

2.2. Candidate Regions: Mean-Shift Segmentation

The approach we propose in this paper is based on analysis of image regions. To obtain candidate regions, we use the mean shift algorithm which is a non-parametric iterative mode-seeking algorithm [FH75] successfully applied in many image processing applications. Let $\{\mathbf{x}_i\}_i$ be a set of n points in R_d, a d-dimensional space. We denote by $\hat{f}(\mathbf{x})$ the multivariate density kernel estimate computed at point $\mathbf{x}$ as follows:

$$\hat{f}(\mathbf{x}) = \frac{1}{nh^d} \sum_{i=1}^{n} K\left(\frac{\mathbf{x} - \mathbf{x}_i}{h}\right) \tag{2}$$

where $K(\mathbf{x})$ is the kernel and h the window radius. The optimal kernel yielding minimal mean integrated square error is the multivariate Epanechnikov kernel. Its expression is given by:

$$K_E(\mathbf{x}) = \begin{cases} \frac{1}{2} c_d^{-1}(d+2)(1 - \|\mathbf{x}\|^2) & if\ \|\mathbf{x}\| < 1 \\ 0 & otherwise \end{cases} \tag{3}$$

where c_d is the volume of the unit d-dimensional sphere. The mean-shift procedure consists in modifying each point $\mathbf{x}_i$ iteratively until convergence using the following equation:

$$\mathbf{x}_i^{(t+1)} = \mathbf{x}_i^{(t)} + \mathbf{m}(\mathbf{x}_i^{(t)}) \ \ where \ \ \mathbf{m}(\mathbf{x}) = \frac{h}{d+2} \frac{\hat{\nabla} f(\mathbf{x})}{\hat{f}(\mathbf{x})}.$$

Candidate regions are then determined using the dynamic mean shift algorithm proposed by [ZKT06].

2.3. The *a contrario* framework

The *a contrario* approach is a mathematical formalization of a perceptual grouping principle. Its application to image analysis has been developed by Desolneux *et al.* [DMM03]. In our context within the *a contrario* framework, the observation model in the absence of outliers is called the *a contrario* model. The purpose of the *a contrario* model is to define outliers (e.g. MS lesion regions) as events of very low probability. Mathematically, this has been formalized by Desolneux *et al.* [DMM03] as follows: *An event of type "such configuration of geometric objects has such property" is ϵ-meaningful if the expectation of the number of occurrences of this event is less than ϵ under the uniform random assumption*.

Let F denote the inverse cumulative probability distribution function of a change measure X under the null hypothesis $\mathcal{H}_0$ (no lesion). This function is defined as $F(\nu) = P(X > \nu)$, the probability that the local measure exceeds a given threshold ν under $\mathcal{H}_0$. Let ν_i , $i = 1, ..., N_\nu$ be a set of N_ν thresholds. Let R be a region of n independent voxels. Let k_i denote the observed number of points (in region R) at which the measure exceeds ν_i. Considering the event $E_{\nu_i,R}$ = "at least k_i points of the region R of size n assume an observation measure larger than threshold ν_i", the probability of event $E_{\nu_i,R}$ is

$$P(E_{\nu_i,R}) = \sum_{j=k_i}^{n} \left(\begin{array}{c} n \\ j \end{array} \right) F(\nu_i)^j (1 - F(\nu_i))^{n-j} \tag{4}$$

(i.e. the tail of the binomial distribution). It is important to note that the event $E_{\nu,R}$ is defined considering a *region* of points. This means that the decision takes into account spatial context. Considering N_R regions in the image, a region R is said to be ϵ-meaningful if:

$$N_R . N_\nu . \min_i P(E_{\nu_i,R}) \leq \epsilon \tag{5}$$

The quantity $N_R . N_\nu . \min_i P(E_{\nu_i,R})$ is called the "Number of False Alarms" (NFA) in the *a contrario* framework. The NFA corresponds to the expectation of false alarms under $\mathcal{H}_0$. In practice, ϵ is often set to 1, meaning that one false alarm on average is expected in the *a contrario* model when testing N_R regions and N_ν thresholds [DMM03]. In our previous work [RFHA+07], we have shown that it is possible to modify Equation 5 in order to get a more flexible decision threshold, using for instance the False Discovery Rate proposed by Benjamini and Hochberg [BH95].

Partial volume artefacts are a well-known issue when using GMM to model brain tissues. These artefacts are taken into account by replacing in Equation 4 k_i by $k(Var(\mathbf{x_i}))$ which is a function of the local variance at the voxel $\mathbf{x_i}$. The higher the local variance, the lower the value of $k(Var(\mathbf{x_i}))$.

In the context of MS lesion segmentation, the probability density function of the *a contrario* model is known and corresponds to the estimated GMM. To determine automatically the threshold ν, we consider that a voxel $\mathbf{x_i}$ is an outlier of the GMM by computing the Mahalanobis distance $\delta(\mathbf{x_i}, c_j)$ between $\mathbf{x_i}$ and each class c_j of the estimated finite GMM: $\delta(\mathbf{x_i}, c_j) = (\mathbf{x_i} - \mu_j)^T \Sigma_j^{-1} (\mathbf{x_i} - \mu_j)$. $\delta(\mathbf{x_i}, c_j)$ gives a measure of how the voxel $\mathbf{x_i}$ fits the model. The Mahalanobis distance under some assumptions on the noise distributions and some first-order approximations, is a random variable with a χ^2 probability distribution. By consulting a table of values of the χ^2 distribution, it is then easy to determine a confidence level ϵ for δ corresponding to, for instance a 95% probability of having the distance δ less than ϵ. A voxel $\mathbf{x_i}$ is considered

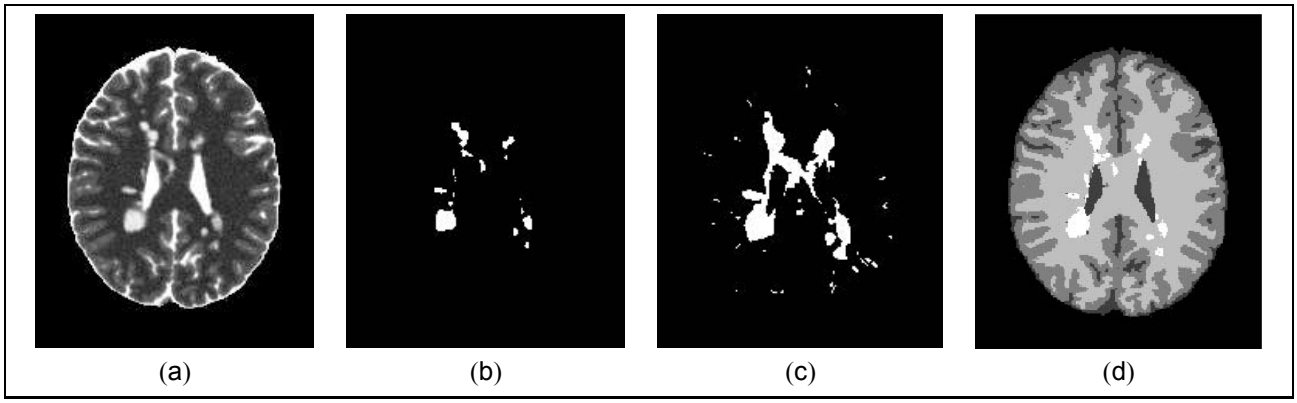

Fig. 1. (a) : BrainWeb T2-weighted image with severe simulated MS lesions, (b) : crisp lesions, (c) : binary mask of fuzzy lesions, (d) : result with the proposed region-based approach.

as an outlier if it does not fit the model for every class c_j of the GMM. Then, we compute for each region the probability of event $E_{\nu,R}$ and we are able to decide whether the considered region is an outlier or not.

3. EXPERIMENTS

One of the main problems in validating automatic algorithms for change detection is the lack of gold standard. To evaluate our approach, we first use simulated images from the BrainWeb simulator [CKKE97]. We evaluate the proposed approach using BrainWeb T2-weighted and T1-weighted synthetic 3D MR images with three types of lesions (mild, moderate, severe), 3% noise level and $1mm$ slice thickness (see for instance Figure 1).

The kappa index (KI) is usually used to evaluate a segmentation algorithm: $KI(R, GT) \triangleq \frac{2\sharp(R \cap GT)}{\sharp R + \sharp GT}$. GT stands for the ground truth map, R is the segmentation result. This index provides information about overlap between segmentation results and a ground truth. However, boundaries of MS lesions are often unclear. Concerning BrainWeb simulated MR images, MS lesions are simulated using smooth profiles. A crisp version $\mathcal{C}$ and a fuzzy version $\mathcal{F}$ of MS lesions are provided. Computing the KI between segmentation results and $\mathcal{C}$ may introduce a bias in the evaluation of the segmentation algorithm, since $\mathcal{C}$ is an under-estimation of lesion load. As it shown in Figure 1, the use of the binary masks of $\mathcal{C}$ or $\mathcal{F}$ will lead to very different values of KI. It appears that the single value of KI is not enough to evaluate a lesion segmentation algorithm. Moreover, the value of KI is very dependent on the size of segmented regions.

A satisfactory result $\mathcal{R}$ of a segmentation algorithm can be defined by the two following conditions: 1) $v \in \mathcal{C} \Rightarrow v \in \mathcal{R}$, 2) $v \in \mathcal{R} \Rightarrow v \in \mathcal{F}$. Thus, we propose to evaluate the segmentation results using the following criteria: $KI(R, \mathcal{C})$, $\max_i\{KI_i(R, \mathcal{F}_i)\}$ where $\mathcal{F}_i$ is a binary map of $\mathcal{F}$ using threshold i, number of undetected connected components (i.e. lesions) with respect to $\mathcal{C}$, number of connected components which are false alarms with respect to $\mathcal{F}$. Results are presented in Table 1. In the context of the revised "McDonald Criteria" for MS diagnosis, it is fundamental to estimated the dissemination in space of MS lesions. Since the KI is very dependent on the lesion size, analysis of lesion segmentation as connected components is more adapted. Results show good performances of the algorithm on the BrainWeb data set.

The algorithm has been tested on our clinical database. MR data sets were acquired on a Philips scanner (T1-weighted: repetition time (TR) $TR = 21ms$, echo time (TE) $TE = 3.75ms$, $2mm$ slice thickness; FLAIR: $TR = 11909ms, TE = 100ms$, inversion time (TI) $TI = 2000ms$, $2mm$ slice thickness). Before applying the proposed method, we use the following preprocessing steps: bias-field correction with the N3 algorithm [SZE98], brain extraction with the BET algorithm [S02] and affine registration to ensure spatial correspondance. The method shows good results as presented in Figure 2.

4. CONCLUSION

We have proposed in this paper a new region-based approach relying on the original *a contrario* framework to detect MS lesions as outliers of a model of brain tissue intensities in multimodal MR data. We have also pointed out that the evaluation of MS lesion segmentation is not straightforward and should be done carefully. Future work focuses on on-going validation studies and the incorporation of particular knowledge of MS lesion locations using statistical atlases.

5. REFERENCES

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	Kappa Index with Crisp Lesions	Maximum Overlap with Fuzzy Lesions	Number of Undetected Lesions	Number of False Alarms	Number of Crisp Lesions
Mild	0.52	0.65	2	1	13
Moderate	0.63	0.71	7	1	59
Severe	0.82	0.86	0	0	39

Table 1. Results for BrainWeb simulated data (using three types of MS lesions : Mild, Moderate and Severe).

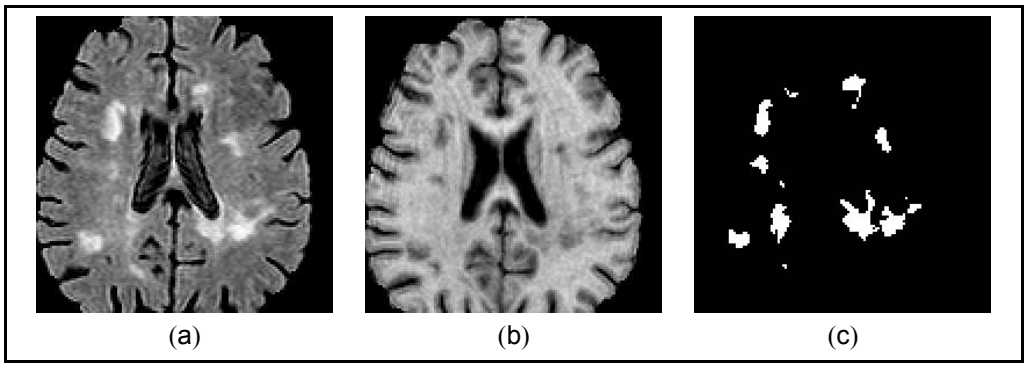

Fig. 2. Clinical data. (a) : Flair image, (b) : T1-weighted image, (c) : resulting mask of MS lesions.

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